



INDIAN HEALTH SERVICE
National Pharmacy and Therapeutics Committee
Formulary Brief: Geriatric Drug Safety & Deprescribing
-April 2023-



Background:

The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) provided a clinical review of Geriatric Medication Safety and Deprescribing. Guidance from the American Geriatrics Society's Beers Criteria and World Health Organization, as well as several medication deprescribing protocols/screening tools were profiled and highlighted individually. Following review and deliberation, **the NPTC made no modifications to the National Core Formulary.**

Discussion:

The category of elderly is typically defined as patients aged 65 years old and older. Elderly patients have both pharmacokinetic and pharmacodynamic differences than their younger counterparts. Age-related changes in pharmacokinetics include changes in distribution due to proportional increase in body fat relative to skeletal muscle, decreased hepatic metabolism, and decreased renal function. As a result, drug half-lives and plasma concentrations can be increased.¹ Pharmacodynamic differences include increased sensitivity to the effects of benzodiazepines, opioids, anticholinergics, and other CNS active medication.² Rates of end-stage renal disease increase by 10% annually for American Indian/Alaskan Natives (AIAN) compared to 6% for whites.³ Another important issue, elder abuse, can manifest as neglect, malnourishment, over/under medication and medication diversion from the elderly.⁴

Geriatric syndromes are common health conditions in elderly patients that do not fit into distinct, organ-based disease categories and which often have multifactorial causes. Geriatric syndromes include cognitive impairment, delirium, incontinence, malnutrition, falls, gait disorders, pressure ulcers, sleep disorders, sensory deficits, fatigue, and dizziness.⁵ Falls are an especially impactful geriatric syndrome. The CDC's Behavioral Risk Factor Surveillance System found that 28% of adults aged ≥ 65 years reported at least one fall, that falls increased to $\sim 34\%$ in those aged ≥ 85 years, and that 10% reported a fall-related injury within the past year. Notably, nearly 95% of all hip fractures are caused by falls. Between 25 to 75% of community-living adults who have a hip fracture do not recover to their pre-injury functional status. Fall-related injuries are the leading cause of death from injury in the elderly and the fifth-leading cause of death overall. Medication use is one of the most modifiable risk factors for falls. Certain medications, including potentially inappropriate medications (PIMs), and sheer volume of medications (polypharmacy) are noted to increase fall risk potential. Fall risk increases when patients have frequent dose changes or have poor medication adherence. Drugs affecting the central nervous system (CNS) are commonly associated with falls. One meta-analysis found the likelihood of falling increased with sedatives and hypnotics (OR 1.47, 95% credible interval [CrI] 1.35-1.62), neuroleptics and antipsychotics (OR 1.59, 95% CrI 1.37-1.83), antidepressants (OR 1.68, 95% CrI 1.47-1.91), and benzodiazepines (OR 1.57, 95% CrI 1.43-1.72).⁶

PIMs are medications where the potential risks outweigh the benefits when prescribed to elderly patients. A list of PIMs, also known as the Beers List, was first published by the American Geriatrics Society in 1991. The most recent update to the [Beers list was published 2019](#), and an update is expected this year. Authors to the Beers List reach expert consensus using the Delphi Method and the Beers List incorporates strength of recommendation and quality of evidence. The 2019 update to the Beers List is organized into 7 different tables which guide a determination of the risk of various pharmacotherapeutic agents.

Another list which can help facilitate the optimization of a medication regimen is the STOPP/START List (Screening Tool of Older Persons' Prescriptions, Screening Tool to Alert doctors to Right Treatment). This was first published in 2008 and contains both a list of PIMs (i.e., STOPP) and medications that patients should be taking (i.e., START). A more recent update was published in 2014 and is known as [STOPP/START "Version 2"](#). It is organized into 4 different appendices which are further divided into sections, including evidence-to-recommendations and STOPP/START criteria. In the acute care and long-term care settings, the STOPP/START lists have been shown to reduce both the use of PIMs and falls, and decrease length-of-hospital stay and costs. However, evidence for its usefulness in community practice are not as strong and, originating from Europe, not all recommendations may be as relevant to prescribing practices in the U.S.^{7,8}

Some especially problematic and commonly prescribed PIMs include anticholinergic medications, benzodiazepines, antipsychotics, and proton pump inhibitors (PPIs). From 2005 to 2009, 23% of community-dwelling persons aged ≥ 65 years with dementia were prescribed medications with clinically significant anticholinergic activity. Many adverse effects associated with anticholinergic use in older adults have similarities to geriatric syndromes including memory impairment, confusion, and hallucinations. The risk of dementia and Alzheimer's disease increases in a dose-response relationship with use of anticholinergic medications. Utilization of the Drug Burden Index can assist with discovering the impact of additive anticholinergic effects. Benzodiazepines increase the risk of falls, delirium and other cognitive dysfunction, acute respiratory failure when used with opioids, dependence, withdrawal symptoms, and potentially dementia. Antipsychotics

are often used for the management of the behavioral and psychological symptoms of dementia, despite limited evidence. Antipsychotic medications are consistently among the drugs most frequently associated with adverse events in long-term care facilities. The FDA has issued a Black Box Warning for antipsychotics due to fatal adverse events in demented patients treated with atypical antipsychotic therapy. Older adult patients with dementia were found to be 1.6 times more likely to die when given atypical antipsychotic therapy than those given placebo, with mortality differences noted in as little as 30 days of initiation. Conventional antipsychotics are as bad as, if not worse, than atypical antipsychotics.^{1,6,10} Roughly 47% of patients taking PPIs are aged ≥ 65 years. Therapy often starts in the inpatient setting. Approximately 70% of the time, PPIs are initiated without an appropriate indication. Adverse events associated with PPIs include fractures (RR 1.33, 95% CI: 1.15-1.54), pneumonia (OR 1.27, 95% CI: 1.11-1.46), clostridium difficile infections (OR 1.73, 95% CI: 1.47-2.85), and vitamin B12 deficiency (OR 1.95, 95% CI: 1.77-2.15). The 2019 update to the Beers List recommends avoiding treatment with an PPI for longer than eight weeks if possible.^{2,10,11}

Polypharmacy is another medication-related modifiable risk factor. Although there is no standardized definition, polypharmacy is often defined as the routine use of five or more medications, including OTCs, herbals, and traditional medications. Polypharmacy can be further classified as appropriate or inappropriate, as not all polypharmacy is avoidable. From 2017 to 2019, over 90% of Emergency Department visits in the U.S. attributed to medication harms in elderly patients were for medications prescribed for a therapeutic use. All medications on an elderly patient's profile should be assessed for appropriateness and potential optimization. A World Health Organization report on polypharmacy estimated that inappropriate polypharmacy contributed to 4% of the world's total avoidable costs due to suboptimal medicine use. Approximately \$18 billion, or 0.3% of global total health expenditures could be avoided by appropriate polypharmacy management. An internal review of IHS National Data Warehouse data from 2008 found that nearly 50% of elderly patients receiving care in the IHS take 4 or more medications.^{12,13,14}

The U.S. Department of Veterans Affairs (VA) has developed a deprescribing methodology to reduce PIMs and polypharmacy known as VIONE. Elements of the VIONE system include Vital (life-saving medications), Important (improve quality of life), Optional (no major impact whether taken or not), Not Indicated (treatment complete), and Every medication has a diagnosis/indication. This methodology reduces polypharmacy by identifying and discontinuing unnecessary, ineffective, and inappropriate medications. VIONE is integrated as part of the VA's Electronic Health Records (EHR) system. It can be used across any VA patient care setting and medical providers and pharmacists can deprescribe PIMs, while engaging patients, care takers, and/or other health care professionals. The VIONE method is currently active in 122 VA medical center programs. As a result of utilization of VIONE, over 1,000,000 unique prescription orders have been discontinued. The estimated annualized cost avoidance is \$100 million as of March 9, 2023.¹⁵

Other external approaches to assist deprescribing efforts include the STOPP methodology (STOPPFall and STOPPFrail). STOPPFall is organized by medications class and incorporates a fall risk assessment, tapering, and post-deprescribing recommendations. STOPPFrail is organized similarly to the standard STOPP list but incorporates frailty and life expectancy as considerations to its deprescribing recommendations. The goals of STOPPFrail include optimizing quality of life and minimizing drug-related morbidity.^{16,17}

Findings:

Elderly patients have different pharmacokinetic and pharmacodynamic parameters than younger adults. As a result, elderly patients may have increased exposure to medication risk. Elderly patients are especially sensitive to CNS active medications, especially anticholinergics, benzodiazepines, and anti-psychotic medications. Medication regimens should be optimized to minimize PIMs, adverse drug effects, and drug-drug interactions. Polypharmacy, which typically defined as the common use of 5 or more medications (including OTCs, herbals, and traditional medications) should be assessed and minimized if possible. Deprescribing strategies such as VIONE, STOPPFall and STOPPFrail provide frameworks which can help decrease PIMs and polypharmacy.

References:

1. Rochon PA, Schmader KE, Givens J. [Drug prescribing for older adults](#). UpToDate. Updated: Nov 07, 2022.
2. By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. [American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults](#). J Am Geriatr Soc. 2019; 67(4):674-694.
3. Hendrix, L, PhD. [Health and health care of American Indian Older Adults](#). In Periyakoil VS, eds. eCampus-Geriatrics, Stanford CA, 2010.
4. Crowder J, Burnett C, Byon HD, et al. [Exploration and Comparison of Contextual Characteristics and Mistreatment Prevalence Among Older American Indian and Alaska Native Respondents](#) J Interpers Violence. 2022; 37(3-4):1456-1483.
5. Ward KT, Reuben DB, Schmader KE, et al. [Comprehensive geriatric assessment](#). UpToDate. Updated: Jul 22, 2022.
6. Kiel DP, Schmader KE, Givens J. [Falls in older persons: Risk factors and patient evaluation](#). UpToDate updated: May 20, 2022.
7. Isenor JE, Bowles SK. [Clinical Pharmacy Considerations in Special Populations: Geriatrics](#). Editor(s): Zaheer-Ud-Din Babar, Encyclopedia of Pharmacy Practice and Clinical Pharmacy, Elsevier, 2019, Pages 803-814.
8. STOPP-START version 2. [Tools to guide which medicines should be considered for deprescribing](#). Health Quality & Safety Commission. New Zealand Government. Updated April 2022. Accessed 4/17/2022.
9. Airagnes G, Pelissolo A, Lavallée M, et al. [Benzodiazepine Misuse in the Elderly: Risk Factors, Consequences, and Management](#). Curr Psychiatry Rep. 2016; 18(10):89.

10. Leszcynski L, Bente J. [Development and Implementation of a Pharmacist-Led Proton Pump Inhibitor Deprescribing Algorithm in a Geriatric Ambulatory Office](#). Sr Care Pharm. 2023; 38(3):105-112..
11. Aubert CE, Blum MR, Gastens V, et al. [Prescribing, deprescribing and potential adverse effects of proton pump inhibitors in older patients with multimorbidity: an observational study](#). CMAJ Open. 2023; 11(1):E170-E178.
12. Budnitz DS, Shehab N, et al. [US Emergency Department Visits Attributed to Medication Harms, 2017- 2019](#). JAMA. 2021;326(13):1299-1309.
13. World Health Organization. [Medication Safety in Polypharmacy](#). Geneva; 2019 (WHO/UHC/SDS/2019.11). License: CC BY-NC-SA 3.0 IGO.
14. Berger L, et. al. [Identifying Polypharmacy among Older Adults Using IHS National Data Warehouse Data](#). The IHS Provider (2010): 239-41.
15. Battar, S. [Medication Deprescribing Methodology for Planned Cessation of Non-Essential Medications](#). VIONE - Medication Optimization and Polypharmacy Reduction Initiative. Va.gov. Updated March 2023.
16. Isenor JE, Bowles SK. [Clinical Pharmacy Considerations in Special Populations: Geriatrics](#). Editor(s): Zaheer-Ud-Din Babar, Encyclopedia of Pharmacy Practice and Clinical Pharmacy, Elsevier, 2019, Pages 803-814.
17. Seppala LJ, Petrovic M, Ryg J, et al. [STOPPFall \(Screening Tool of Older Persons Prescriptions in older adults with high fall risk\): a Delphi study by the EuGMS Task and Finish Group on Fall-Risk-Increasing Drugs](#). Age Ageing. 2021 Jun 28;50(4):1189-99.